Remarks

Claims 1, 3-6, 8-14, 16, 17 and 19-26 were pending. Claims 6, 12, 14, 17, 20-21 and 25 are amended herein. Claims 14, 20 and 21 are amended to correct syntax, as suggested in the Office action. Claims 9 and 17 are amended herein to remove reference to trademarks. Claims 6, 9, 12 and 14 are amended herein to incorporate the limitations of claim 1. Support for the amendments to claims 17 and 24-25 can be found throughout the specification, such as, but not limited to, page 10.

Claim 11 is canceled herein. New claims 27-28 are added herein. Support for new claims 27-28 and can be found throughout the specification and in claims 23 and 24.

Following entry of this amendment, claims **1, 3-6, 8-10, 12-14, 16, 17 and 19-28** are pending. Applicants believe no new matter is added herein. Reconsideration of the subject application is respectfully requested.

Specification

The specification was objected to for including references to trademarks that were not capitalized, and was objected to for not including generic terminology for trademarks. Submitted herewith is a replacement specification amended to (1) capitalize trademarks; (2) indicate trademark registration, and (3) provide generic terminology. Applicants believe that the submission of the replacement specification renders the objection moot.

Claim Objections

Claims 14, 20 and 21 were objected to for including improper syntax. Claims 14, 20 and 21 are amended herein as suggested by the Examiner, rendering the objection moot.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 9, 12, 17 and 20 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting a trademark.

Prior to entry of this amendment, claim 9 recited "BETASERON." Claim 9 is amended herein to replace "BETASERON" with the generic name, "interferon-beta 1b," thereby rendering the rejection moot.

Claims 12, 17 and 20 also were rejected for including a recitation of a trademark. Applicants assume that the Office action is referring to the recitation of "daclizumab" in these claims. However, "daclizumab" is the generic name for the specific antibody marketed under the trademark "ZENAPAX®." Submitted herewith is the data sheet (exhibit A) from Roche, showing both the trademarked name ("ZENAPAX®) and the generic name ("daclizumab") and describing the sterile concentrate as prepared for injection. This data sheet documents that daclizumab is the generic name for ZENAPAX®. In view of this information, reconsideration and withdrawal of the rejection of claims 12, 17 and 20 are respectfully requested.

Claims 6, 9, 12 and 14 are rejected under 35 U.S.C. § 112, second paragraph for not providing sufficient antecedent basis for the limitation "the interleukin-2 receptor antagonist." Claims 6, 9, 12 and 14 are amended herein to recite "antibody that specifically binds the interleukin 2 receptor" thereby rendering the rejection moot.

Rejection Under 35 U.S.C. § 103

Claims 1, 3-6, 8-14, 16-17 and 19 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the "Study of Zenapax," Khoury et al., Paty et al., and Jacobs et al. Applicants respectfully disagree with this rejection.

"Study of Zenapax" describes a clinical study to examine the safety and effectiveness of Zenapax (also known as "daclizumab") for the treatment of MS. "Study of Zenapax" does not disclose any conclusions regarding the safety and efficacy of Zenapax for the treatment of MS. Thus, one of skill in the art would not conclude that Zenapax would be a safe or effective treatment for MS based on the disclosure of the "Study of Zenapax".

Khoury et al. discloses that the presence of activated T lymphocytes correlates with the progression of multiple sclerosis. As noted in the Office action, Khoury et al. does not describe the effect of interferon beta or Zenapax.

Paty et al. describes the administration of interferon-1 beta-1b to patients with multiple sclerosis. Paty et al. do not teach or suggest the use of any additional agents with interferon-1 beta-b for the treatment of multiple sclerosis.

Jacobs et al. teaches the administration of interferon-1 beta-1a to patients with multiple sclerosis. Jacobs et al. do not teach or suggest the use of any additional agents with interferon-1 beta-1a for the treatment of multiple sclerosis.

The Office action alleges that as Paty et al. and Jacobs et al. teach that interferon-beta 1b and interferon-beta 1a are known to be treatments for multiple sclerosis, one of skill in the art would be motivated to combine these teachings with the disclosure of the study of Zenapax, in view of Khoury et al. Applicants respectfully disagree with this rejection.

To establish a *prima facie* case of obviousness (1) there must be some suggestion in the reference or knowledge generally available to one of ordinary skill in the art to modify the reference or combine the references; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. MPEP § 2143.

The Patent Office has not established a *prima facie* case of obviousness. At a minimum, there is no suggestion in the "Study of Zenapax" that the use of daclizumab is safe or effective for the treatment of MS, alone or in combination with an additional agent. This deficiency is not cured by Paty et al or Jacobs et al which fail to suggest a combination of interferon beta with an anti-IL2 receptor antibody for the treatment of MS. Accordingly, the Patent Office has failed to establish a motivation to combine the cited references. The mere fact that a reference can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Furthermore, given success rate of clinical trials, a person of skill in the art would not have a reasonable expectation of success that the combination of Zenapax with interferon beta would be successful for the treatment of MS. As set forth in the Declaration of Dr. Alice Fong, the reduction in the number of new lesions following treatment with daclizumab would not have been predicted based on prior results. Dr. Alice Fong describes results obtained in a multi-center, randomized, double-blind,

placebo controlled clinical trial that was performed at 51 sites, both in the U.S. and abroad. This study was designed to investigate the effect of concurrent daclizumab and interferon-beta therapy in patients with active relapsing remitting multiple sclerosis (MS). In this study, patients with multiple sclerosis (MS) were treated using one of three treatment protocols: (1) daclizumab (Roche Penzberg) at 2 mg/kg subcutaneously every two weeks with concurrent interferon-beta therapy; (2) daclizumab at 1 mg/kg subcutaneously every four weeks with concurrent interferon beta therapy (a placebo was administered every two weeks, to alternate with daclizumab); and (3) placebo every two weeks with concurrent interferon beta therapy (control group). The primary efficacy endpoint was the number of new or enlarged gadolinium contrast enhancing lesions on monthly brain MRIs between week 8 and week 24 of the study. Statistical analyses were used to study the efficacy of the treatment regimens. Individuals in Group (1), who received 2 mg/kg daclizumab every two weeks had a 72% reduction ($p=0.004$) in the mean number of new or enlarged gadolinium contrast enhancing lesions as compared to the control group (who received only interferon-beta). Individuals in Group (2), who received 1 mg/kg daclizumab every four weeks had a 25% reduction ($p=0.501$) in the mean number of new or enlarged gadolinium contrast enhancing lesions as compared to the control group (who received only interferon-beta). Thus, treatment with daclizumab in combination with interferon-beta provided an unexpected reduction in the number of gadolinium contrast enhancing lesions than treatment with interferon-beta alone. This finding of an unexpected result overcomes any prima facie case of obviousness based on Pay et al, Jacobs et al., Study of Zenapax and Khoury et al.

Reconsideration and withdrawal of the rejection of claims 1, 3-6, 8-14, 16-17 and 19 under 35 U.S.C. § 103 are respectfully requested.

Obviousness-Type Double Patenting

Claims 1-21 and 29-34 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-21 and 29-34 of co-pending U.S. Patent Application No. 10/607,598. U.S. Patent Application No. 10/607,596 has issued as U.S. Patent No. 7,258,859 (hereinafter the '859 patent).

The claims in the '859 patent are directed to the treatment of a subject with multiple sclerosis with a therapeutically effective amount of daclizumab (1) *in the absence of treatment with beta interferon, wherein (2) the subject has failed to respond to previous treatment with beta interferon.*

The claims of the present application are directed to treatment of subjects with multiple sclerosis with a therapeutically effective amount of daclizumab *in combination with* therapeutically effective amount of interferon-beta.

The claims of the present application and the claim of the '859 patent are patentably distinct (and do not overlap in scope) with the claims of the present application. As the claims of the '859 patent recite that daclizumab must be administered in *the absence of interferon* they *teach away* from the combined use of daclizumab and interferon-beta for the treatment of multiple sclerosis. Furthermore, the claims of the '859 patent are directed to the treatment of subject who have failed to respond to previous treatment with interferon-beta. If a subject has failed treatment with a therapeutic agent is not obvious to administer that same therapeutic agent, either alone or in combination with any other agent.

Reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

Applicants believe the present application is ready for allowance, which action is requested. If any matters remain to be discussed before a Notice of Allowance is issued, or if an action on the merits will be issued, Examiner Hissong is respectfully requested to contact the undersigned for a telephone interview at the telephone number listed below.

Respectfully submitted,

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